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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,363	11/09/2001	Daria Mochly-Rosen	58600.8209.US00	3578

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PERKINS COIE LLP
P.O. BOX 2168
MENLO PARK, CA 94026

EXAMINER	
SNEDDEN, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1653	9

DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/007,363	MOCHLY-ROSEN, DARIA	
	Examiner	Art Unit	
	Sheridan K Snedden	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *12-22,25 and 26* is/are pending in the application.

4a) Of the above claim(s) *19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-18, 20-22, 25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. This Office Action is in response to Paper #7, filed 23 June 2003. Claims 1-11, 23 and 24 have been canceled. Applicant's amendment of claims 12, 13, 15-17, 22, 25 and 26 is acknowledged. Claims 12-18, 20-22, 25 and 26 are under examination.

Withdrawal of Objections and Rejections

2. The objections and/or rejections not explicitly restated or stated below are withdrawn.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-18, 20-22, 25 and 26 rejected under 35 U.S.C. 103(a) as being unpatentable over Liang *et al.* (US Patent 6,329,349) in view of Dorn *et al.* (IDS).

Liang *et al.* teach reducing ischemic injury of the heart via sequential administration cardioprotective agents (see column 2, lines 10-35). These methods entail the administration of cardioprotective agents to a patient prior to surgical treatment followed by administration of a second cardioprotective agent to potentiate the cardioprotective effect. This second cardioprotective agent is delivered to the patient either before, during or after surgery. Alternatively, the second cardioprotective agent may be administered continuously throughout

all of these periods (see column 2, lines 10-22; regarding claims 1-6 and 12-17). The cardioprotective agents are delivered to the patient, and therefore to the cells and tissue, by direct perfusion of the organ or by intravenous administration (regarding claims 11, 22, 24, 25 and 26). Liang *et al.* also suggest intracoronary administration of cardioprotective agents (see column 1, lines 42-46, and reference 1 therein; regarding claim 26). Figure 2 shows that the period of ischemia was 90 minutes (regarding claims 3, 5, 14 and 16). Therefore, Liang *et al.* teaches all of the method steps of the present invention, however, does not teach the use of psi-epsilon-RACK peptides as cardioprotective agents.

Dorn *et al.* teach a composition of a psi-epsilon-RACK peptide (HDAPIGYD) identical to SEQ ID NO: 2. Dorn *et al.* teach that the psi-epsilon-RACK peptide caused cardio-protection from ischemia (regarding claims 1 and 7). The study of Dorn *et al.* was conducted by prior administration or expression of the psi-epsilon-RACK peptide to cardiac myocyte cells or whole hearts *ex vivo* that have undergone ischemic exposure for 30 minutes (see Experimental Procedures, pages 12798-99; regarding claims 1-3, 7, 12-14, 18, 23 and 25). Additionally, Dorn *et al.* teach an Antennapedia carrier peptide identical of SEQ ID NO: 3 (see Experimental Procedures; regarding claim 9 and 10). Dorn *et al.* do not teach the administration of the above cardioprotective peptide after or during the exposure to a cell or tissue (regarding claims 4-6 and 15-17). Additionally, Dorn *et al.* do not teach in vivo administration by the routes consisting or intravenous, intracoronary, parenterally, subcutaneous, inhalation, intranasal, sublingual, mucosal, or transdermal administration of the above cardioprotective peptide (regarding claims 11, 22, 24, and 26).

Taken together the above references teach the administration of the cardioprotective psi-epsilon-RACK peptide or SEQ ID NO: 2 linked to the Antennapedia carrier peptide for reducing injury to a cell using the method steps recited in the claims of the present invention. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to utilize the psi-epsilon-RACK peptide (Dorn *et al.*) in the method of reducing ischemic injury of the heart via the sequential administration of cardioprotective agents as taught by Liang *et al.* As the psi-epsolon-RACK peptide of the instant invention and agents of Liang *et al.* possess the identical cardioprotective effect, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute one for another. A person of ordinary skill in the art would have been motivated and expected success to make the above substitution as a synergistic effect would have been observed using a combination of cardioprotective agents that function via different mechanisms, as suggested by Liang *et al.* Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

a. Applicant argues that the use of peptides as therapeutic agents is fraught with problems and limited by delivery problems and that Liang *et al.* does not teach the administration of peptides. Applicant further states that obviousness requires an expectation of success, which requires at least some degree of predictability. Applicant argues that Dorn *et al.* does not teach administering to an organ *in vivo* a $\psi\epsilon$RACK peptide, and does not suggest that the peptide could be administered for therapeutic activity.

b. Applicant's arguments have been fully considered but they are not persuasive. Dorn *et al.* expresses the ψεRACK peptides in transgenic mice and demonstrates the ability of the peptide to protect against ischemic injury. Chronic expression in a transgenic mouse would read upon the recitation of 'administering to an organ in vivo a ψεRACK peptide'. Dorn *et al.* do suggest that the transgenic mouse is a model demonstrating the therapeutic potential ψεRACK peptides or like drugs in cardiac ischemia. Therapeutic activity from the endogenous overexpression of ψεRACK peptides in mice would suggest that an exogenous titer of the peptide would also demonstrate therapeutic value.

Applicant's arguments concerning the predictability of peptides as therapeutic drugs are considered but are not persuasive. It is common knowledge in the art that peptides have therapeutic value and may be exogenously administered for exploitation of their therapeutic effect to an organ in vivo. Such examples are insulin, growth hormone, Epo, and hemoglobin to name a few. As such, an expectation of success and a degree of predictability does exist. The rejection in maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (703) 305-4843. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone number for regular communications to the organization where this application or proceeding is assigned is (703) 746-3975.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SKS
September 22, 2003

SKS

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER